



4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2000-D-0598 (formerly 2000D-1631)]

International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH GL23(R)); Studies to Evaluate the Safety of Residues of Veterinary Drugs in Human Food: Genotoxicity Testing; Revised Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a revised guidance for industry (GFI) #116 entitled “Studies to Evaluate the Safety of Residues of Veterinary Drugs in Human Food: Genotoxicity Testing” (VICH GL23(R)).

This revised guidance has been developed for veterinary use by the International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH). In this VICH guidance, the recommendation for a second test to evaluate the potential of a chemical to produce chromosomal effects is revised. The revised guidance indicates that the potential of a chemical to produce chromosomal effects can be evaluated using one of the following three tests: (1) An in vitro chromosomal aberrations test using metaphase analysis, which detects both clastogenicity and aneugenicity; (2) an in vitro mammalian cell micronucleus test, which detects the activity of clastogenicity and aneugenicity; or (3) a mouse lymphoma test,

which, with modification, can detect both gene mutation and chromosomal damage. This revised VICH guidance document is intended to facilitate the mutual acceptance of safety data necessary for the establishment of acceptable daily intakes for veterinary drug residues in human food by the relevant regulatory authorities.

DATES: Submit either electronic or written comments on Agency guidance at any time.

ADDRESSES: Submit written requests for single copies of the revised guidance to the Policy and Regulations Staff (HFV-6), Center for Veterinary Medicine, Food and Drug Administration, 7519 Standish Pl., Rockville, MD 20855. Send one self-addressed adhesive label to assist that office in processing your request. See the SUPPLEMENTARY INFORMATION section for electronic access to the revised guidance document.

Submit electronic comments on the revised guidance to <http://www.regulations.gov>.

Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Tong Zhou, Center for Veterinary Medicine (HFV-153), Food and Drug Administration, 7500 Standish Place, Rockville, MD 20855, 240-402-0826, Tong.Zhou@fda.hhs.gov.

SUPPLEMENTARY INFORMATION:

I. Background

In recent years, many important initiatives have been undertaken by regulatory authorities and industry associations to promote the international harmonization of regulatory requirements. FDA has participated in efforts to enhance harmonization and has expressed its commitment to seek scientifically based, harmonized technical procedures for the development of pharmaceutical products. One of the goals of harmonization is to identify, and then reduce,

differences in technical requirements for drug development among regulatory agencies in different countries.

FDA has actively participated in the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) for several years to develop harmonized technical requirements for the approval of human pharmaceutical and biological products among the European Union, Japan, and the United States. The VICH is a parallel initiative for veterinary medicinal products. The VICH is concerned with developing harmonized technical requirements for the approval of veterinary medicinal products in the European Union, Japan, and the United States, and includes input from both regulatory and industry representatives.

The VICH Steering Committee is composed of member representatives from the European Commission, European Medicines Evaluation Agency, European Federation of Animal Health, Committee on Veterinary Medicinal Products, FDA, the U.S. Department of Agriculture, the Animal Health Institute, the Japanese Veterinary Pharmaceutical Association, the Japanese Association of Veterinary Biologics, and the Japanese Ministry of Agriculture, Forestry, and Fisheries.

Six observers are eligible to participate in the VICH Steering Committee: One representative from the government of Australia/New Zealand, one representative from the industry in Australia/New Zealand, one representative from the government of Canada, one representative from the industry of Canada, one representative from the government of South Africa, and one representative from the industry of South Africa. The VICH Secretariat, which coordinates the preparation of documentation, is provided by the International Federation for Animal Health (IFAH). An IFAH representative also participates in the VICH Steering

Committee meetings.

In the Federal Register of March 5, 2013 (78 FR 14306), FDA published a notice of availability for a draft revised guidance document entitled “Studies to Evaluate the Safety of Residues of Veterinary Drugs in Human Food: Genotoxicity Testing” (VICH GL23(R)) giving interested persons until May 6, 2013, to comment on the draft revised guidance. FDA received one comment on the draft revised guidance, and that comment, as well as those received by other VICH member regulatory agencies, were considered as the guidance was finalized. The guidance announced in this document finalizes the draft revised guidance dated March 5, 2013. The revised guidance is a product of the Safety Expert Working Group of the VICH.

This revised VICH guidance document recommends a second test to evaluate the potential of a chemical to produce chromosomal effects. The revised VICH guidance indicates that the potential of a chemical to produce chromosomal effects can be evaluated using one of the following three tests: (1) An in vitro chromosomal aberrations test using metaphase analysis, which detects both clastogenicity and aneugenicity; (2) an in vitro mammalian cell micronucleus test, which detects the activity of clastogenicity and aneugenicity; or (3) a mouse lymphoma test, which, with modification, can detect both gene mutation and chromosomal damage. This revised VICH guidance is intended to facilitate the mutual acceptance of safety data necessary for the establishment of acceptable daily intakes for veterinary drug residues in human food by the relevant regulatory authorities. The objective of this revised VICH guidance is to ensure international harmonization of genotoxicity testing.

II. Significance of Guidance

This guidance, developed under the VICH process, is being issued consistent with FDA’s good guidance practices regulation (21 CFR 10.115). This guidance represents the current

thinking of FDA on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

III. Paperwork Reduction Act of 1995

This guidance refers to previously approved collections of information found in FDA regulations. These collections of information are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). The collections of information in 21 CFR part 514 have been approved under OMB control number 0910-0032.

IV. Comments

Interested persons may submit either electronic comments regarding this document to <http://www.regulations.gov> or written comments to the Division of Dockets Management (see ADDRESSES). It is only necessary to send one set of comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday, and will be posted to the docket at <http://www.regulations.gov>.

VI. Electronic Access

Persons with access to the Internet may obtain the revised guidance at either <http://www.fda.gov/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/default.htm> or <http://www.regulations.gov>.

Dated: May 7, 2015.

Leslie Kux,

Associate Commissioner for Policy.

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